REMARKS

Initially, applicants note that the only amendments to the claims were submitted in the preliminary amendment filed June 11, 2001, and that, contrary to an indication in the office action, no amendments to the present claims were submitted on September 13, 2001.

After entry of this amendment, claims 1, 2, 4-18 and 20 will be pending. Claim 1 has been revised to prescribe a sterol as part of the recited "saponin component," and to include the elements previously set forth in claim 3, now canceled. Claims 2, 6, and 7 have been amended in order that consistent terminology is used throughout the claims. Claims 4, 8 and 10-12 have been amended to depend from claim 2. Claim 8 also has been revised to recite a single range and to employ terminology tracking that of base claim 1. Claim 17 has been amended to use consistent terminology with claim 13. Claims 3 and 19 have been canceled without prejudice in this amendment solely to advance the prosecution of this application. Claim 20 has been added.

The foregoing claim amendments and cancellations are made without prejudice and solely to advance to prosecution of this application.

Support for the amendments to the claims can be found throughout the application as originally filed, including, but not limited to: claim 1 -- page 10, lines 9-15 and originally filed claim 3; and claim 20 -- original claim 8. Thus, the present do not add new matter and otherwise are proper. Applicants respectfully request entry of this amendment in its entirety.

In view of the above amendments and following remarks, applicants respectfully request reconsideration of the claims and submit that the application is in condition for allowance. This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, are presented, with an appropriate defined status identifier.

I. Claim Rejections – 35 U.S.C. §112, Second Paragraph

In the office action, claims 8-12, 16 and 19 were "rejected as being indefinite," based on the use of apparently inconsistent terminology. Specifically, claims 8, 10-12 and 16 recited "immunostimulating complex" while claims 2 and 6-7 recited "immunostimulatory complex." Claims 2 and 6-7 have been amended to recite immunostimulating complex. Claims 10-12 and 16 also were deemed "unclear because [the immunostimulating complex's] relationship to the saponin component of base claim 1 has not been defined." Claims 10-12 have been amended to depend from claim 2 which specifies the relationship between the saponin component and the immunostimulating complex.

Applicants respectfully submit that the recitation of "immunostimulating complex" in claim 16 is definite. First, claim 16 refers to an "immunostimulating complex," not "the immunostimulating complex," and thus introduces this element for the first time in this series of claims. Second, "immunostimulating complexes " are discussed in the application as filed, and the metes and bounds of what constitutes an immunostimulating complex are clear to the skilled artisan. Finally, one skilled in the art would recognize not only that immunostimulating complexes can contain saponin but also that saponins can be used as adjuvants in the absence of an immunostimulating complex. Therefore, it would be clear to the skilled artisan that the saponin could either be separate from, part of, or both separate from and part of the immunostimulating complex of claim 16.

Claim 8 was rejected for reciting multiple ranges. Claim 8 has been amended to recite a single range.

Claim 19 was rejected for failing to recite "any active, positive steps[.]" Claim 19 was also rejected as an improper "process claim under 35 U.S.C. 101." Claim 19 has been canceled rendering this ground for rejection moot.

In light of the above amendments and comments, applicants respectfully request the Examiner withdraw these rejections.

II. Claim Rejections – 35 U.S.C. §102

In the office action, claims 1, 3-5, 13-14 and 17-19 were "rejected under 35 U.S.C. 102(b) as being entirely anticipated by James *et al.* (WO 88/07547)," claims 1, 3-5, 13-14 and 17-19 were rejected "as being entirely anticipated by Moss *et al.* (WO 91/04052)," and claims 1, 3-5, 13 and 17-10 were rejected "as being entirely anticipated by Edgar *et al.* (WO 99/27959)." Applicants respectfully traverse these rejections. Claim 3 has been canceled rendering these rejections moot with respect to claim 3. Additionally, claims 4, 5, 10, 11 or 12 are not anticipated by any of these references because these claims are now dependent on claim 2, which the Examiner explicitly recognized was not anticipated by the cited references. Accordingly, applicants respectfully request the Examiner withdraw the anticipation rejection as they relate to claims 3, 4, 5, 10, 11 and 12.

The cited references also cannot anticipate claims 1, 13-14 and 17-19 because none teaches each and every element of the claimed invention. The present claims specify that the composition comprises a saponin component that includes a sterol. None of the cited references even hints at using a saponin component that includes a sterol. Neither James *et al.* nor Edgar *et al.* makes any mention of a sterol. Although Moss *et al.* disclose that cholesterol can be used as a "filler" in their vaccine composition (see, e.g., page 12, line 5), the cholesterol of Moss *et al.* does not form part of a saponin component as claimed in the present invention.

The present claims specify that adjuvant has two individual components, the polysaccharide component and the saponin component. The saponin component is made up of at least two sub-components, the saponin and the sterol. Examples of such saponin components are described in the specification at page 10, lines 1–20 and include immunostimulating complexes and their derivatives. The present invention can be illustrated by P+S or P+s's", where P is the polysaccharide, s' is the saponin, s" is the sterol and S is the saponin component (which is the same as s's" together).

In sharp contrast, Moss *et al.* only teach a "solid vaccine" that includes "an antigenic substance capable of inducing the generation of antibodies on parenteral administration to an

animal, a saponin and a polycationic adjuvant" (page 5, lines 4-9). The vaccine of Moss *et al.* can also contain a filler and a "filler which may be used is cholesterol" (page 12, line 5). Thus, Moss *et al.* describe a vaccine containing, at a minimum, an antigenic substance, a saponin, a polycationic adjuvant and, optionally, a filler which can be cholesterol. Schematically this can be illustrated as A+Sa+Poly+Ch where A is the antigen, Sa is saponin, Poly is the polycationic adjuvant, and Ch is cholesterol. This illustration below clearly shows the differences between the present invention and Moss *et al.*

Present Invention	**Moss *et al.***
P+**S** or P+**(s's")**	A+**Sa**+Poly+**Ch**

In the present invention, at least the saponin and the sterol combined (s's") make up the single saponin component of the present adjuvant (S), whereas the saponin (Sa) and cholesterol (Ch) of Moss *et al.* are separate components. This difference is clearly illustrated as well by comparing the present application with Moss *et al.* In the present application the saponin component is part of the adjuvant composition. Accordingly, the saponin component is an individual component that can be present prior to the introduction of any immunogen to the adjuvant. On the contrary, the cholesterol filler of Moss *et al.* is added to the vaccine, if at all, only *after* the antigen, saponin and polyanionic adjuvant are mixed together and dried. For instance, see the examples of Moss *et al.*

Because Moss *et al.* add the saponin and cholesterol at different times they can never form the single saponin component of the present claims. Accordingly, Moss *et al.* fail to teach or suggest all of the elements of the present claims. Because the cited references do not teach all of the elements of the present claims, applicants respectfully request that the Examiner withdraw these rejections.

III. Claim Rejection – 35 U.S.C. §103

Claims 1 and 13-15 stand rejected as obvious "over James *et al.* or Moss *et al.*, either in view of McNamara (WO 99/02180)." In traversal, Applicants first note that original claim 3 was

not rejected as obvious over any combination of the cited references, that the elements of claim 3 have been included in claim 1, and that all claims ultimately depend from claim 1. Accordingly, the present claims are not obvious over the combined references. Moreover, this rejection fails to state a *prima facie* case of obviousness because the cited references fail to teach or suggest all of the elements of claim 1. MPEP § 2143.03.

As discussed above, neither primary reference suggests an adjuvant that has an ionic polysaccharide component and a saponin component made up of a saponin and a sterol. McNamara cannot overcome this deficiency because that reference fails to suggest any composition containing a sterol. Applicants respectfully request, therefore, that the Examiner withdraw this rejection.

Claims 1-2, 6 and 7 were rejected as obvious over "over James *et al.* or Moss *et al.*, either in view of MacKenzie *et al.* (4,981,684)." Applicants respectfully traverse this rejection. They have noted already that the elements of claim 3, which was not rejected as obvious, have been included in the claim 1 rendering the claims nonobvious over the cited references. In addition, the combination of Moss *et al.* and MacKenzie *et al.* is improper because there is no motivation to the skilled artisan to combine the references which, in fact, teach away from their combination.

As discussed above, Moss *et al.* is directed solely to "a solid vaccine composition" (page 5, line 5). Nowhere do Moss *et al.* disclose that there vaccine can be used in any other than a solid form. In contrast, MacKenzie *et al.* teach a method for forming iscoms without the removal of a solubilizing agent. As discussed by MacKenzie *et al.*, iscoms are prepared in solution to form defined, art recognized structures which are administered in solution. For instance, see column 3, lines 12-25, and column 4, lines 54-66. Nowhere do the references teach or suggest that the iscoms of MacKenzie *et al.* are suitable for use in solid vaccine preparations of Moss *et al.* Combining Moss *et al.* with MacKenzie *et al.* is improper, therefore. For the stated reasons, applicants respectfully request the Examiner withdraw these rejections.

CONCLUSION

In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

Respectfully submitted,

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By _____

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